Claim 20 has been amended to state that construct components are operably joined, as suggested by the Patent Office. New Claim 43, submitted in place of cancelled Claim 29, includes similar language.

Claims 24-26 have been amended to refer to the promoter region as upstream of the TATTTAA site, as was stated in Claims 8-10 as originally filed. Applicants note that the original claim language incorrectly included sequence 3' to the TATTTAA region in the stated promoter sizes. The current language correctly recites the numbers of bases upstream of the TATTTAA region that were used in exemplified constructs. Support for the FMV 34S promoter regions recited in Claims 24 and 25 is found at page 9, lines 1-10 (196bp and 362bp upstream from TATTTAA, respectively). Support for the FMV 34S promoter region recited in Claim 26 finds support at page 8, lines 14-15 and in Figure 4. Although the number of base pairs is not specifically stated in the specification, one skilled in the art would readily determine that the indicated *Eco*RI site (first 6bp of Figure 4 sequence) is 892bp 5' of the TATTTAA site at bases 894 to 900 of Figure 4.

Additional amendments to Claims 20, 22-26, 30 and 35-36 are in response to various rejections raised in the Office Action. Support for new Claim 43 is found in Claims 13-14 as filed, and in the specification at page 7, beginning at line 20.

Claims 21 and 31 have been cancelled in view of amendment to Claim 20 and the language of new Claim 43. Claims 32 and 37-42 have been cancelled in the interest of furthering prosecution of the instant application.

It is readily apparent that no new matter is added in the above amendments to the claims, and the Examiner is respectfully requested to enter them in the instant application. These amendments are believed to place the claims in condition for allowance, and in any event are necessary to put the application in better condition for appeal. The amendments were not earlier presented because they are in response to rejections first presented to Applicants in the Final Office Action mailed March 19, 1992.

35 U.S.C. 112, Second Paragraph Rejection

Claims 20-42 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

The rejection of Claim 20 is believed avoided by the above amendment to Claim 20 which states that the components are operatively joined and provides a 3' transcript termination region as a component of the transcription constructs. Similar language is presented in new Claim 43 submitted in place of cancelled Claim 29.

The rejection of Claim 22 is believed avoided by amendment to replace "untranslated end" with --flanking region--.

Amendments to Claims 24-26 replace "upstream" with --5' region-- for purposes of clarification, and remove the phrase "approximately". In addition, comments at page 3 of the Office Action and discussions during the Examiner interview as to the use of the term "promoter" were considered in amendments to Claims 24-26. The amendments clarify that Applicants' invention

includes constructs which comprise the promoter region upstream of the TATTTAA, as stated in Claims 8-10 as originally filed. As noted by the Examiner in the Office Action of March 19, 1992 and discussed in the Examiner interview, the sizes of the promoter regions originally stated in Claims 8-10 were incorrect, as they referred to the promoter plus a portion of the 5' untranslated region. The rejection of Claims 33-34 is respectfully traversed as these claims now correctly refer to recombinant constructs that "further comprise a 5' untranslated leader sequence", in view of the above discussed amendment to Claim 20.

The rejection of Claims 29-32 is believed avoided in new Claim 43, and Claim 30, dependent thereon. Claim 43 clarifies that the instant invention includes a DNA cassette which comprises two chimeric gene constructs, a first construct wherein a DNA sequence of interest is regulated by an FMV 34S promoter region, and a second DNA construct wherein a DNA sequence of interest is regulated by a CaMV 35S promoter. As described in the specification at pages 7 and 26, such DNA cassettes are valuable in genetic engineering applications where <u>two strong promoters</u> are required. The use of the non-homologous FMV and CaMV promoters assures high levels of expression in both DNA constructs and avoids DNA recombination problems that might occur were the 35 promoter to be used in two different constructs. In response to comments in the Office Action, no structural orientation between the FMV and CaMV constructs in the DNA cassette is intended, other than that the components of each promoter construct are operably joined, as stated, so as to

provide for transcription of their respective DNA sequences of interest.

35 U.S.C. 112, First and Second Paragraphs

The rejection of Claims 20 and 23-26 are believed avoided by amendment of these claims to state a figwort mosaic virus 34S promoter.

35 U.S.C. 102

Claims 20-21, 23-27 and 33-34 were rejected under 35 U.S.C. 102(b) as anticipated by Richins *et al*. This rejection is respectfully traversed as follows.

Prior art anticipates a claim only if every element recited in the claim is disclosed in a single item of prior art. Richins *et al*. does not fulfill this requirement for the invention as presently claimed. The current claims are directed to recombinant DNA constructs which comprise as operably linked components, a figwort mosaic virus promoter and a DNA sequence of interest heterologous to the FMV promoter. Thus, only DNA constructs which comprise these elements as operatively joined components could be considered to anticipate the instantly claimed invention. There is no disclosure of such constructs in Richins *et al*., which merely reports the insertion of FMV *Xba*I fragments into cloning vectors. There is no indication that a figwort mosaic virus *Xba*I fragment comprising the FMV 34S promoter was inserted in position for transcription of the ß-galactosidase gene. Furthermore, this reference clearly does not

teach constructs which further comprise a plant functional transcription termination region, as stated in the present claims.

In view of the above, Applicants respectfully request that the rejection under 35 U.S.C. 102(b) be withdrawn.

35 U.S.C. 103

Claims 20-42 were rejected under 35 U.S.C. 103 over the combination of Shah *et al.* and Sanders *et al.* taken with Richins *et al.* and Shepherd et al. This rejection is respectfully traversed as follows.

Shah *et al.* describe DNA constructs for expression of EPSPS gene sequences in plant cells. As noted in the Office Action, this reference does not teach or suggest the figwort mosaic virus 34S promoter of the instant invention.

Sanders *et al.* compares the strength of CaMV 35S and nopaline synthase (nos) promoters in leaves from transgenic plants and discusses the higher level of expression obtained with the 35S promoter. Again, there is no teaching or suggestion of a figwort mosaic virus 34S promoter.

Richins *et al.* is more relevant to the instantly claimed invention, in that a figwort mosaic virus is studied. However, this reference does not provide one with the instantly claimed invention. The authors only speculate as to the location of figwort mosaic virus promoters, but do not provide any convincing evidence of the claimed figwort mosaic virus 34S promoter of the instant invention. Prior to Applicants' teachings in the instant

application, there was insufficient evidence for one skilled in the art to predict, with a reasonable expectation of success, the instantly claimed invention.

In addition to the lack of demonstration of transcription from the putative promoter region and the lack of significant DNA homology to the CaMV 35S promoter region, a close examination of the Richins reference demonstrates that other significant differences in the structural organization of the indicated FMV region as compared to the CaMV 35S promoter. For example, Richins notes that the suggested TATA region in the figwort mosaic virus sequence occurs just inside the 3' end of the region VI open reading frame. In fact, the suggested TATA box actually contains the TAA stop codon of the region VI structural gene. This is not true for the CaMV 35S promoter, where the TATA box is located in an intergenic region downstream of the CaMV gene VI stop codon. Thus, one skilled in the art could reasonably assume that translational constraints from the region VI structural gene sequence might take precedence over any possible promoter activity in this region. Furthermore, although a TATA element is noted in the disclosed sequence, no CAAT box is not found in the indicated FMV region. The CAAT box is another element commonly associated with plant promoters, and in particular is present in the CaMV 35S promoter region.

Richins' *et al.* predictions about figwort mosaic virus activity were based solely upon knowledge of 35S promoter activity in the only other previously studied member of the caulimovirus group, CaMV. As evidence that one can not, from a

single example, extrapolate results to other caulimovirus strains, Applicants submit a reference, Hasegawa *et al.* (*Nucl. Acids Res.* (1989) *17*:9993-10013), which reports studies with another member of this plant virus group. The authors describe a new promoter activity in the soybean chlorotic mottle virus (SoyCMV) from a region IV upstream fragment and note that no such activity has been reported for other caulimoviruses, even though "promoter-like signals" are present in this location of CaMV.

Thus, in view of the lack of predictability in caulimovirus studies, the lack of extensive sequence homology to the CaMV 35S promoter region, the absence of the CAAT concensus sequence, and the fact that the entire putative FMV promoter sequence is under transcriptional constraints from the gene VI structural gene region, it was not obvious that the predictions of Richins would in fact lead one to a useful plant promoter region.

Shepherd *et al.* is cited by the Patent Office as demonstrating broad host range and high titer obtainable with FMV in plant host cells. The Patent Office cites this reference as providing motivation to study FMV as a promoter source, by characterizing viral titer determinations as providing a basis for predicting high promoter activity from the FMV 34S promoter. Applicants submit that no proven relationship between the aggressiveness of a plant virus and the strength of a given viral promoter has been demonstrated. In fact, Shepherd notes that the most striking changes in the genomes of the low and high-titer FMV strains studied, were in the region that corresponds to the region VI gene, not in the region that corresponds to the FMV 34S

promoter of the instant invention. Furthermore, the FMV 34S promoter characterized in the instant application is derived from a low titer strain of FMV (strain M3 discussed in Shepherd), yet has strong promoter activity comparable to that of the higher titer CaMV 35S promoter. Thus, there appears to be no basis for the Patent Office's conclusion that FMV viral titer can be used to predict the FMV 34S promoter strength.

In view of the above, Applicants respectfully request that the rejection under 35 U.S.C. 103 over the combination of Shah *et al.* and Sanders *et al.* taken with Richins *et al.* and Shepherd *et al.* be withdrawn.

Conclusion

In view of the above Amendments and remarks, it is respectfully submitted that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (916) 753-6313.

Respectfully submitted,

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